Psoriasis

The Poster Child for Bench-to-bedside Translational Medicine

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ABSTRACT

As the largest and most visible organ, the skin provides opportunities to investigate immune responses in clinical studies offering insights that extend beyond our protective coat. The interplay between bench-to-bedside approaches are complemented by bedside-to-bench exchanges epitomizing translational medicine. Conversations beyond improvement in skin lesions that include the impact on patients' lives and well-being are also becoming more frequent. Just as advances in the realm of cutaneous oncology earned malignant melanoma the title of poster child for personalized cancer therapy, new advances involving psoriasis are pointing to this moniker in dermatology once again. In this commentary, the successful cycle of interactions between psoriasis patients, dermatologists, immunologists, and the pharmaceutical industry are highlighted. Lessons learned from psoriasis-based studies indicate a bright future for translational medicine based in dermatology research labs and clinics. (*J Clin Aesthet Dermatol.* 2015;8(7):14–16.)

Psoriasis is a serious medical condition with both physical and emotional components.[1] The advances in understanding the immunopathogenesis of psoriasis are reflected by progress in the clinic for patients with moderate-to-severe plaque stage disease. As psoriasis is a purely human disease,[2] it should not be surprising that many key discoveries during the past two decades resulted from close interactions between patients willing to donate tissue/blood samples and participate in clinical trials, skilled dermatologists involved in the clinical trial arena, and researchers working at the bench, all of whom contributed to the success story and rapid progress of translational medicine in the psoriasis field.[3] Figure 1 highlights these close and productive links between psoriasis patients, healthcare providers, researchers, and the pharmaceutical companies to develop optimal treatment for this human-specific disease.

As we evaluate the momentum gained over the past two decades, it is worth pausing to place this progress in perspective. Analogous to recent successes in personalized therapies in the cutaneous oncology field, where translational-guided approaches led to optimal treatment selection for patients with melanoma (being declared the poster child for personalized therapeutics in 2010),[4] the common auto-inflammatory chronic skin malady, psoriasis, is assuming the mantle of poster child for translational medicine in dermatology. As recently summarized by Drs. Menter and Griffiths, the future is bright for psoriasis therapy, thanks to greater understanding of various psoriasis subtypes and application of personalized therapy approaches.[5]

There is evidence that psoriasis as a chronic illness may impact a patient's quality of life to a similar degree as major medical illnesses, such as cancer.[6] Moreover, a growing body of literature indicates that psoriasis can significantly impact many aspects of a patient's life quality.[7] These findings support increasing focus on the evaluation of the patient's perspective when conducting clinical trials beyond assessments of signs and symptoms. The most widely used and clinically validated tool for this patient assessment is the dermatology life quality index or DLQI.[8] By asking the patient directly how the therapy is affecting their quality of life, this patient-centric approach complements more common evaluations, such as Psoriasis Area and Severity Index (PASI) and Physician's Global Assessment (PGA), which are traditionally regarded by physicians as important measures of therapeutic response. This 10-item questionnaire takes only 5 to 10 minutes to complete, provides the basis for constructive and informative conversations in the clinic, and adds an important dimension for advancing our understanding of psoriasis.

Dr. Finlay and colleagues have demonstrated the

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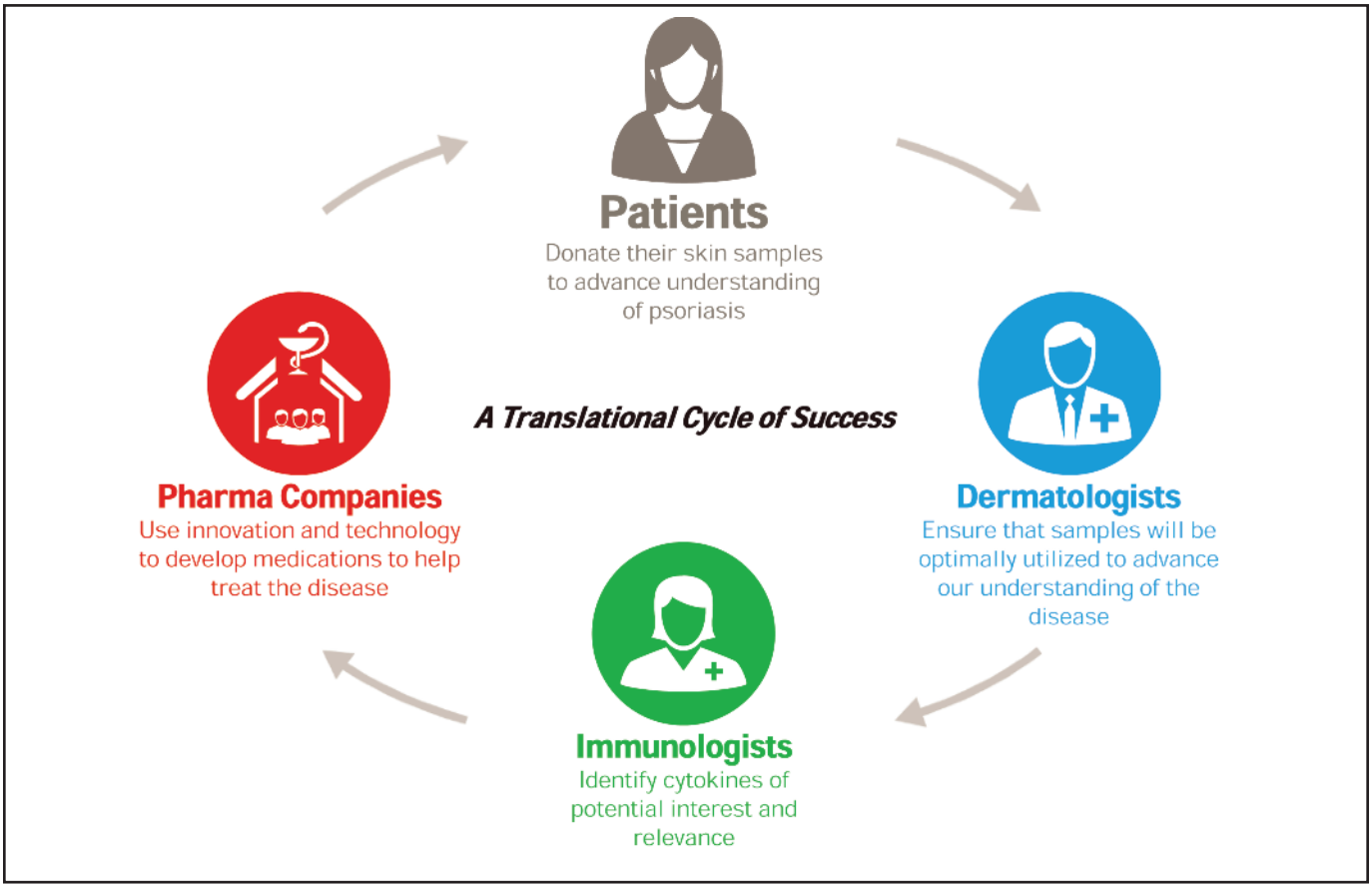

Figure 1. A translational cycle of success by which patients with psoriasis are interconnected with dermatologists, immunologists, and pharmaceutical companies.

importance of properly interpreting an individual's DLQI score in a manner that is optimal for informing clinical decisions.[9] An initial study determined that marked improvements in DLQI scores were found in patients achieving at least a 75-percent improvement from baseline in their PASI scores.[10] With achievement of higher levels of relative clearance of psoriatic lesions during the past several years due to advancements in targeted therapies, we now have the opportunity to more thoroughly probe this relationship by determining how even relatively small levels of residual skin disease can impact life quality. Thus, just as the use of relative improvement in PASI scores has become more commonplace in the clinics, additional studies are not only suggesting the bar be raised from PASI 75 to PASI 90,[11] but greater attention be devoted to the impact of treatments on DLQI. While this will require further investigation and confirmation in future studies, there is an early indication that patients achieving clear skin no longer experience an impact of psoriasis on their quality of life.[11]

A broader appreciation is also developing for the association between the more extensive skin involvement in patients with severe psoriasis and significant comorbidities, including cardiovascular disease.[12] Cardiovascular disease is the main driver of excess mortality in psoriasis,[12] and having severe psoriasis is accompanied by a six-year reduction in life expectancy.[13] Understanding the relationship between chronic inflammation in the skin and inflammation in system-wide organ sites is likely to yield greater insights into a variety of comorbidities that will require appropriate tools to assess the impact on patients' lives. Not only can new research improve our understanding of the relationship between chronic inflammation in the skin and cardiovascular disease, but recently identified central nervous system (CNS)-associated lymphatic vessels, which act as direct conduits between lymph nodes and CNS, may yield further insight into neuroinflammatory disease.[14]

The new revelation of functional conduits (lymphatic vessels) connecting the CNS to the immune system opens a promising line of inquiry as to how these two systems actually communicate. From a dermatology perspective there are many reasons to be intrigued by this topic, given so many skin diseases can be triggered or influenced by stress.[15] Psoriasis may also be considered a poster child for the field of psychoneuroimmunodermatology,[15] beginning with the clinical recognition of a link to stress, the

symmetry of lesion expression,[16] altered innervation patterns in psoriatic skin,[17,18] and importance of innervation in experimental models of psoriasis.[19] While systemic inflammation in patients with severe psoriasis may explain the link to cardiovascular disease, this association might also be mediated by stress and neurological factors, long known to be associated with cardiovascular morbidity.[20]

In conclusion, there is little doubt that psoriasis epitomizes the essence of translational medicine that is impacting not only dermatology, but other medical specialties as well. Because psoriasis manifests itself as visible plaques often associated with numerous comorbidities, and progress continues in both basic and clinical research, studies of psoriasis will continue to provide insights that are likely to extend beyond the skin for many years to come.

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